Proposed Renal and Urological Sciences (RUS) Integrated Review Group
Summary of Public Comments

The Renal and Urological Sciences (RUS) Study Section Boundaries Team met from April 25 - 26, 2002, to design the study sections of the proposed RUS Integrated Review Group (IRG 20) and draft proposed guidelines. These guidelines were made available for public comment on the Center for Scientific Review (CSR) Web site for a 12-week period that ended in September 2002. CSR also received correspondence concerning the organization of this IRG and the feedback from those letters is included in this summary.

GENERAL SUPPORT OR CONCERNS FOR IRG STRUCTURE:

- **CSR received a number of comments supporting the proposed study section organization**

- **Overrepresentation of kidney related research in the guidelines:** There was criticism that the Team over-designed in the area of renal diseases, leaving only one study section to address lower urinary tract research, diseases and dysfunctions. Shown below are examples of the remedies proposed by commenters:

    - Create a 4th study section that focuses on the lower urinary tract and a 5th section that focuses on genital/sexual function. But if there are to be only 3 study sections in the RUS IRG it would be recommended that there be 1 for kidney diseases, 1 for genital/fertility/sexual dysfunction, and 1 for lower urinary tract function. This would also make it easier to recruit study section members who are competent in the areas of all grant applications submitted to each study section.

    - The proposal will not serve the needs of basic and translational scientists focused on non-kidney related urologic disease. Create a study section that would review applications related to bladder, prostate and testicular development, physiology and pathobiology.

    - There would be more balance if study sections were organized as following: (a) Cellular and Molecular Biology of the Kidney; (b) Pathobiology of Kidney and Genitourinary Diseases; (c) Cellular and Molecular Biology of the Genitourinary Tract.

    - The here is a lack of prostate in general. In fact, prostate and bladder are the two most focused organs in the urological research. There needs to be a study section focused on prostate.

    - Poorly supported areas fall farther and farther behind, and the necessary first phase of descriptive research never is completed. Remarkable strides have been made in the past few years since the Urology Special Emphasis Panel has been in existence. Hopefully, this will continue until a second study section is required.

- **Size and workload concern (1):** Concern was expressed that CMBK and PKGD will not have a large pool of applications. …. The advantage for having a broad scientific interest study section is that a healthy number of applications will be reviewed and that the scores are less squeezed in a study section having a large pool of grant application

than those having a small pool. Therefore, it was hoped that CMBK and PKGD could have a broader specific interest than that in the present proposal in order to maintain a large pool size of applications.

- **Size and workload concerns (2)**: If the number of applications for this IRG were larger, these study section guidelines would be very appropriate. As they are they are too small. When study sections are less that 50 applications/cycle, review of application suffers because the reviewers evolve into members of a clique with destructive behaviors that will harm the strength of peer review. Consideration should be given to reducing the number of study sections to two more appropriately sized study sections.

- **Function-driven events:** This current organization is organ system based (the kidney), rather than function based (ion and blood pressure homeostasis, renal filtration, etc.) but homeostasis (and normal healthy function) usually requires a couple of organ systems. Two cases in point: (1) Potassium homeostasis is not managed by just the kidney but also the skeletal muscle; (2) Blood pressure is not managed by just the kidney but also by CV sensors, endocrine systems, and the brain regulation of SNS. …It's not clear what hypertension grants should go to CMBK vs. PBKD vs. Cardiovascular Sciences. The division between these IRGs will create grants that look at renal vs. non-renal aspects when studying multiple systems would be more appropriate.

- **Overall description:** Change paragraph 2 on page one to: .... genetic, cellular and molecular mechanisms of plasma (or maybe better glomerular) filtration, regulation of ... Although glomerular filtration and proteinuria are well covered in the specific areas of PBKD, they should also be emphasized in the overall description of the RUS IRG review area.

- **Clinical research:** The new study section groupings appear reasonable, yet they appear to bury clinical investigation within "more basic" categories of kidney research. It would be useful to specifically identify clinical research within the new three study sections. Use the word "clinical" a lot, so that investigators are encouraged to submit their proposals.

- **Toxicology (1):** Concern was expressed that the fragmentation of toxicological expertise throughout the various new IRGs such that there is no longer a critical mass in any one location to lobby on behalf of the discipline. Toxicology, more than any other area of science, incorporates the utilization of knowledge and techniques from many other disciplines (biochemistry, cell biology, chemistry, pathology, physiology, neuroscience, pharmacology...). It is thus difficult to pigeonhole the discipline of toxicology along the lines of the "organ-system" approach currently being advocated.

- **Toxicology (2):** Perhaps it might make sense to include a Toxicological Sciences Study Section, within the Oncological Sciences IRG since the Oncological Sciences IRG is crosscutting. In this way the multi-disciplinary nature of current toxicology research will be accommodated within an IRG that was specifically designed to respond to the special needs of such multi-disciplinary research.

STUDY SECTION SPECIFIC COMMENTS

Cellular and Molecular Biology of the Kidney

- **Transport systems:** The separation of the transport systems to the CMBK study section is good.

- **Osmoregulation and sensing:** The area of "molecular biology of osmoregulation and osmosensing" should be among the topics covered by this study section.

- **Non-renal model systems:** Non-renal model systems should be included under this description, e.g., flounder urinary bladder, shark rectal gland, red blood cell (water channels, anion exchanger; KCl cotransporter, several others); the use of blood and cultured cells in studies of cellular fluid, electrolyte, and acid base regulation and homeostasis; and lipid bilayer reconstitutions (ENaC and many other channels). CSR is also urged to recognize the continuing importance of heterologous expression systems, including Xenopus oocytes and cultured mammalian cells, in the study of renal function.

- **Mineral metabolism of the kidney:** This was handily covered by GMB. However, with the division of mineral metabolism to ORTH and OBM2, without renal expertise, and RUS with ample kidney expertise but not with calcitropic hormones and receptors, creates a serious gap.

Pathobiology of Kidney Disease (PBKD)

- **Gene therapy and stem cells:** Gene stem cell therapy of kidney disease should be added. Although they have not come of age yet, such approaches to kidney therapy will be increasing in the near future.

- **Kidney development and neoplasia:** Kidney development and neoplasia may be more appropriate in the PBKD section. Disease states such as renal cystic disease, neoplasia and repair following ischemia have many similarities with development. In addition, many researchers have cross interests/expertise in more than one of these areas that would be quite useful during study section discussion of these types of grant proposals.

- **Transplantation:** There is a great risk in fragmenting the review of grants in transplantation to the extent that there will not be adequate peer review. The CSR should publish a formal discussion of what constitutes an appropriate critical mass of grants on a specific subject (i.e., transplantation) and an appropriate representation of true experts in that subject in order for a given study section to qualify for adequate peer review. Public comment on such a discussion should be invited.

- **Acute renal failure:** The locus of review of acute renal failure needs to be clarified.

- **Dialysis Outcomes:** The locus of review of dialysis outcomes research (i.e., analysis of current network data) versus the review of grants to study dialysis-related mechanisms of disease. The former is closer to epidemiology and systems; the latter may have a molecular biology orientation.

- **Dialysis:** CSR is urged to elevate dialysis research to a separate category of its own within PBKD.

Urologic and Kidney Development and Genitourinary Diseases (GKDD)

- **CSR received many comments expressing pleasure with the creation of this study section.**

- **Male reproductive system and infertility research:**

    - CSR received a number of comments, including letters from the Endocrine Society and the Society for the Study of Reproduction, strongly opposing the separation of male and female reproductive and infertility research. In their opinion it would be more appropriate to cluster these areas of research in the proposed Endocrinology, Metabolism, Nutrition and Reproductive Sciences (EMNR) IRG rather than fragment them across multiple IRGs. The respondents argue that the two systems cannot be separated because reproduction cannot occur in the absence of either. Furthermore, members of non-reproductive sciences communities do not have the expertise to properly critique applications and will marginalize reproductive biology applications.

    - Research in the area of male infertility is not well addressed by any of the review panels proposed. For studies that are not endocrine based, but urologic or genetic based (especially in the human) there is no real proper review panel proposed. This was problematic with even the current review system and is now even more so with the changes proposed. For example, investigators working on a signal transduction pathway in germ cells may have their proposal sent to a "signal transduction" focused review panel that has no appreciation for the differences between meiotic and meiotic cells. They may have no interest in the basic mechanisms of spermatogenesis addressed by such studies, even though the experimental focus is appropriate for the panel.

    - Placement of andrology in the RUS IRG casts this discipline as a primarily mechanical entity, and distances male reproductive research from its basic science and internal medicine components. The RUS IRG as currently constituted would not be capable of giving a comprehensive review to applications that went beyond fluid dynamics. The present proposal fragments the urology elements from basic biology and endocrinology. If applications in reproductive science are to be assigned to RUS, fair review will absolutely require substantial representation in its roster of the other disciplines that make up andrology today. If this cannot be done, then they are better off staying in REB or REN, with urology expertise added as needed.

- **Epidemiology:** This IRG covers many subject areas and scientific methodologies, only a subset of which are epidemiology. Proper and fair peer review requires that peers review grants. If NIH seeks to support the best studies in renal and urologic disease epidemiology, and the best investigators in the field, it is critical that study sections with the expertise to understand epidemiology review the epidemiology grant applications.

- **Cancer and translational research:** The GKDD study section should also include cancer. It should encourage the translational aspects of urology research and not just basic science. Thus, it should review grants on disease diagnosis and treatment, including those on genito-urinary tumors

- **Diseases of the Bladder:** Diseases such as overactive bladder (a complex disorder often leading to incontinence) and Interstitial Cell Cystitis should be included in GKDD.

- **Female disorders:** There is an over-emphasis on male-oriented disorders. A major urological disorder, incontinence, is also prevalent in females, and should be given consideration.

- **Sensory and Pain Studies:** Studies related to the generation of pain and the treatment of pain from these organ systems is of great importance. Addition of verbiage specifically about studies that seek to understand sensory processes related to the kidney and urinary tract structures is encouraged.

- **Health Services/Quality-of-Life studies:** The IRG excludes health services and outcomes research in kidney and urologic diseases. These appear to have no home.

- **In vivo modeling of urologic function/dysfunction:** There is little indicating the importance of in vivo modeling of urologic function and dysfunction. Hopefully, this arm of research will be appropriately represented.

NON-IRG OR STUDY SECTION SPECIFIC REMARKS:

In addition to the comments shown above, CSR also received comments pertaining to the review process and the composition of study sections.

- **Reviewers:**

    - Basic science: If there are not enough strong basic scientists, the proposed new IRG could seriously diminish research in the field of male reproductive biology.

    - Clinical: The composition of the study sections that will review applications made to the three new sections are of concern… In the past the study sections were heavily weighted toward basic scientists. This issue is especially important if translational research burgeons over the next two decades.

    - Pathology: A group charged with evaluating, in part, translational projects, should have more individuals involved with a track record in this area. Specifically, there appears to be an under-representation by pathologists who understand the feasibility of achieving such aims**.**

    - SRA flexibility in assembling review committees: Currently, the SRA is able to alter the composition of a given study section meeting depending on the mix of grants that come in (i.e., one time it might be heavy on bladder and another time several impotence grants may be submitted). CSR is urged that the SRA continue to have this flexibility so that the best people can review the grants at any given review panel.

- **Advocating a blind review process:** The major problem is actually not resolved, namely bias by the study section members. The only REAL solution to these biases is to

introduce blinding into the review process. The initial scientific review by study section reviewers should include only the scientific portion of the application.